

What is claimed is:

1. A method of effectively treating benign prostatic hypertrophy in a human patient, comprising:  
administering terazosin transdermally to the human patient by applying a transdermal delivery system containing terazosin to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of said patient for at least 3 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said terazosin within 36 hours from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the three-day dosing interval.
2. The method of claim 1, further comprising providing a mean relative release rate of terazosin from said transdermal delivery system to provide a plasma level of terazosin of at least about 1.0 ng/ml within about 6 hours after application of said transdermal delivery system onto the skin of the patient.
3. The method of claim 1, further comprising maintaining a plasma level of terazosin at steady-state from about 10 to about 60 ng/ml.
4. The method of claim 1, wherein said therapeutic plasma level is maintained from about 1.0 ng/ml to about 60 ng/ml during the dosing interval for said transdermal delivery system.
5. The method of claim 1, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 30  $\mu\text{g}/\text{hour}/\text{cm}^2$  of said transdermal delivery system.
6. The method of claim 1, wherein said transdermal delivery system has a mean relative release rate from about 2.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 20  $\mu\text{g}/\text{hour}/\text{cm}^2$ .

7. The method of claim 1, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 30.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 24 hours; from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 28.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 48 hours; and from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 26.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 72 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of Ethanol:water.

8. The method of claim 1, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 52.8  $\mu\text{g}/\text{cm}^2$  to about 686.4  $\mu\text{g}/\text{cm}^2$  at 24 hours; from about 105.6  $\mu\text{g}/\text{cm}^2$  to about 1372.8  $\mu\text{g}/\text{cm}^2$  at 48 hours; and from about 158.4  $\mu\text{g}/\text{cm}^2$  to about 2059.2  $\mu\text{g}/\text{cm}^2$  at 72 hours, as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

9. A method of effectively treating benign prostatic hypertrophy in a human patient, comprising:  
administering terazosin transdermally to the human patient by applying a transdermal delivery system containing terazosin to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said terazosin within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval.

10. The method of claim 9 wherein the plasma level of terazosin at 48 hours does not decrease by more than 30% over the next 72 hours.

11. The method of claim 9, further comprising maintaining an effective mean relative release rate of said transdermal delivery system to provide a substantially first order plasma level increase of terazosin from the initiation of the dosing interval until about 48 to about 72 hours after the initiation of the dosing interval; and thereafter providing

an effective mean relative release rate to provide a substantially zero order plasma level fluctuation of terazosin until the end of at least the five-day dosing interval.

12. The method of claim 9, further comprising providing a mean relative release rate of terazosin from said transdermal delivery system to provide a plasma level of terazosin of at least about 1.0 ng/ml within about 6 hours after application of said transdermal delivery system onto the skin of the patient.

13. The method of claim 9, further comprising maintaining a plasma level of terazosin at steady-state from about 10 to about 60 ng/ml.

14. The method of claim 9, wherein said therapeutic plasma level is maintained from about 10 ng/ml to about 60 ng/ml during the dosing interval for said transdermal delivery system.

15. The method of claim 9, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 30  $\mu\text{g}/\text{hour}/\text{cm}^2$  of said transdermal delivery system.

16. The method of claim 9, wherein said transdermal delivery system has a mean relative release rate from about 2.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 20  $\mu\text{g}/\text{hour}/\text{cm}^2$ .

17. The method of claim 9, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 30.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 24 hours; from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 28.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 48 hours; and from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 26.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 72 hours; and from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 25.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

18. The method of claim 9, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 52.8  $\mu\text{g}/\text{cm}^2$  to about 686.4  $\mu\text{g}/\text{cm}^2$  at 24 hours; from about 105.6  $\mu\text{g}/\text{cm}^2$  to about 1372.8  $\mu\text{g}/\text{cm}^2$  at 48 hours; and

from about 158.4  $\mu\text{g}/\text{cm}^2$  to about 2059.2  $\mu\text{g}/\text{cm}^2$  at 72 hours; and from about 211.2  $\mu\text{g}/\text{cm}^2$  to about 2745.6  $\mu\text{g}/\text{cm}^2$  at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

- ~~19. A method for lessening the incidence of side-effects in a patient associated with the oral administration of terazosin, wherein the method comprises administering said terazosin in a transdermal delivery system over at least twenty-four hours and thereby lessening the incidence of side effects.~~
- ~~20. The method of claim 19 wherein said terazosin is administered in a transdermal delivery system applied to the skin of a human patient for about 3 to about 5 days.~~
- ~~21. The method of claim 19, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 30  $\mu\text{g}/\text{hour}/\text{cm}^2$  of said transdermal delivery system.~~
22. A transdermal delivery system containing terazosin or a pharmaceutically acceptable salt thereof which provides a mean relative release rate from about 1.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 30  $\mu\text{g}/\text{hour}/\text{cm}^2$  of said transdermal delivery system; a plasma level of terazosin of at least about 1.0 ng/ml by about 6 hours after application of said transdermal delivery system onto the skin of the patient; and a plasma level of terazosin at steady-state from about 10 to about 60 ng/ml.
23. The transdermal delivery system of claim 22, which provides a mean relative release rate from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 30.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 24 hours; from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 28.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 48 hours; and from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 27.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 72 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.
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24. The transdermal delivery system of claim 22, which provides an in-vitro cumulative amount of permeation of from about  $52.8 \mu\text{g}/\text{cm}^2$  to about  $686.4 \mu\text{g}/\text{cm}^2$  at 24 hours; from about  $105.6 \mu\text{g}/\text{cm}^2$  to about  $1372.8 \mu\text{g}/\text{cm}^2$  at 48 hours; and from about  $158.4 \mu\text{g}/\text{cm}^2$  to about  $2059.2 \mu\text{g}/\text{cm}^2$  at 72 hours, as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

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25. The transdermal delivery system of claim 22, comprising a backing layer which is impermeable to the active substance, a pressure-sensitive adhesive reservoir layer, and optionally a removable protective layer, the reservoir layer by weight comprising 20 to 90% of a polymeric matrix, 0.1 to 30% of a softening agent, 0.1 to 20% of terazosin base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% of a solvent for the terazosin or salt thereof.

26. The transdermal delivery system of claim 22, which is a laminated composite comprising (a) a polymer ~~backing layer that is substantially impermeable to terazosin or the pharmaceutically acceptable salt thereof; and (b)~~ a reservoir layer comprising an acrylate or silicone based pressure-sensitive adhesive, 0.1 to 20% of terazosin base or of a pharmaceutically acceptable salt thereof, 0.1 to 30% of an ester of a carboxylic acid acting as a softening agent and 0.1 to 30% of a solvent for terazosin having at least one acidic group.

27. The transdermal delivery system of claim 22, which maintains a plasma level of terazosin at steady-state from about 10 to about 60 ng/ml.

28. A transdermal delivery system comprising terazosin or a pharmaceutically acceptable salt thereof which maintains an effective mean relative release rate to provide a therapeutic blood level of said terazosin within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval.

29. The transdermal delivery system of claim 27, which has a mean relative release rate of terazosin effective to provide a plasma level of terazosin of at least about 1.0

ng/ml by about 6 hours after application of said transdermal delivery system onto the skin of the patient.

30. The transdermal delivery system of claim 27, which maintains a plasma level of terazosin at steady-state from about 10 to about 60 ng/ml.

31. The transdermal delivery system of claim 27, wherein said therapeutic plasma level is maintained from about 1.0 ng/ml to about 60 ng/ml during the dosing interval for said transdermal delivery system.

32. The transdermal delivery system of claim 27, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{hour}/\text{cm}^2$  to about 30  $\mu\text{g}/\text{hour}/\text{cm}^2$  of said transdermal delivery system.

33. The transdermal delivery system of claim 27, wherein said transdermal delivery system has a mean relative release rate from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 30.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 24 hours; from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 28.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 48 hours; and

from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 26.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 72 hours; and from about 1.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  to about 25.0  $\mu\text{g}/\text{cm}^2/\text{hr}$  at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

34. The transdermal delivery system of claim 27, wherein said transdermal delivery system provides an in-vitro cumulative amount of permeation of from about 52.8  $\mu\text{g}/\text{cm}^2$  to about 686.4  $\mu\text{g}/\text{cm}^2$  at 24 hours; from about 105.6  $\mu\text{g}/\text{cm}^2$  to about 1372.8  $\mu\text{g}/\text{cm}^2$  at 48 hours; and from about 158.4  $\mu\text{g}/\text{cm}^2$  to about 2059.2  $\mu\text{g}/\text{cm}^2$  at 72 hours; and from about 211.2  $\mu\text{g}/\text{cm}^2$  to about 2745.6  $\mu\text{g}/\text{cm}^2$  at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell has a receptor chamber containing a 40:60 mixture of ethanol:water.

35. The transdermal delivery system according to claim 25, wherein the backing layer is composed of a flexible material.

36. The transdermal delivery system according to claim 25, wherein the backing layer is selected from the group consisting of a flexible material, an inflexible material, and an aluminum foil.

37. The transdermal delivery system according to claim 25, wherein the polymeric matrix is at least one of rubber, a rubber-like synthetic homo-, co- or blockpolymer, a urethane and silicone.

38. The transdermal delivery system according to claim 25, wherein the softening agent is at least one of dodecanol, undecanol, octanol, a glycol and glycanol.

39. The transdermal delivery system according to claim 25, wherein the solvent is a monoester of a dicarboxylic acid.

40. The transdermal delivery system according to claim 25, wherein the solvent is at least one of monomethyl glutarate and monomethyl adipate.

41. The transdermal delivery system according to claim 25, wherein the polymer is a copolymer of 2-ethylhexyl acrylate, vinyl acetate and acrylic acid, the softening agent is dodecanol and the solvent is monomethyl glutarate.

42. The transdermal delivery system according to claim 25, wherein by weight the polymer is present in about 55%, the terazosin in about 10%, the solvent in about 10% and the softener in about 15%.

43. A transdermal delivery system according to claim 25, wherein the solvent is present in from about 25 to 100% the weight of the terazosin.

44. The transdermal delivery system according to claim 25, which also comprises a removable protective layer.

45. The transdermal delivery system according to claim 25, wherein the pressure-sensitive adhesive reservoir layer comprises a polymer based on an acrylate, a methacrylate or a combination thereof.

46. The transdermal delivery system according to claim 25, wherein the softening ester is a medium-chain triglyceride of the caprylic/capric acids of coconut oil.

47. The transdermal delivery system according to claim 25, wherein the solvent has at least one acidic group.

48. The method of claim 19, wherein said transdermal delivery system has a mean relative release rate from about ~~2.0 µg/hour/cm<sup>2</sup>~~ to about 20 µg/hour/cm<sup>2</sup>.